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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/726,899	11/29/2000	Olga Bandman	PF-0187-2 DIV	3562

7590 03/21/2002

Legal Department
Incyte Genomics, Inc.
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EXAMINER	
ROARK, JESSICA H	
ART UNIT	PAPER NUMBER
1644	9

DATE MAILED: 03/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No. 09/726,899	Applicant(s) BANDMAN ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/7/01 (received 1/3/02)* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *12-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 November 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 11/7/01 and received 1/3/02 (Paper No. 8), is acknowledged.
Claims 1-2, 5-6, 8 and 14 have been amended.
Claims 1-14 are pending.

Claims 1-11 (in part), and 12-14 stand withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1-11 (only with respect to SEQ ID NO:3) *are under consideration in the instant application.*

2. Applicant's comments, filed 11/7/01 reiterating their traversal of the restriction requirement set forth in Paper No.3 and request for rejoinder if an allowable product claim is identified are acknowledged.

It is noted that the restriction requirement was made final in Paper No. 6.

In view of the rejections set forth below, the request for rejoinder continues to be held in abeyance.

3. In order to facilitate the prosecution of this application, Applicant is again requested to amend the claims to delete the non-elected embodiments from the claims.

4. This Office Action will be in response to applicant's arguments, filed 11/7/01 (Paper No. 8).
The rejections of record can be found in the previous Office Action (Paper No. 6).

It is noted that New Grounds of Rejection are set forth herein.

5. Applicant's comments, filed 11/7/01, regarding the objection to the specification as failing to provide proper antecedent basis for the claimed subject matter are acknowledged.

Applicant argues that because the specification indicates that the methods steps are those well known in the art (e.g., page 29 at lines 1-2) and provides non-patent literature that is incorporated by reference describing methods of producing antibodies (e.g., pages 29-30); that this is sufficient to support the instantly recited method steps, at least when considered in view of the description of polyclonal antibody production on pages 52-53 of the specification.

However, the incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See In re Hawkins, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

An application as filed must be complete in itself in order to comply with 35 U.S.C. 112; however this does not bar incorporation by reference. Ex parte Schwarze, 151 USPQ 426 (Bd. of Appeals, 1966). An application for a patent when filed may incorporate "essential material" by reference to (1) a United States patent or (2) an allowed U.S. application, subject to the conditions set forth below. "Essential material" is defined as that which is necessary to (1) support the claims, or (2) for adequate disclosure of the invention (35 U.S.C. 112). "Essential material" may not be incorporated by reference to (1) patents or applications published by foreign countries or regional patent offices, to (2) non-patent publications, to (3) a U.S. patent or application which itself incorporates "essential material" by reference or to (4) a foreign application. See In re Fouche, 169 USPQ 429; 439 F.2d 1237 (CCPA 1971).

Nonessential subject matter may be incorporated by reference to (1) patents or application published by the United states or foreign countries or regional patent offices, (2) prior filed, commonly owned U.S. applications or (3) non-patent publications, for purposes of indicating the background of the invention or illustrating the state of the art.

The referencing application must include (1) an abstract, (2) a brief summary of the invention, (3) an identification of the referenced patent or application, (4) at least one view in the drawing in those applications admitting of a drawing, and (5) one or more claims. Particular attention should be directed to specific portions of the referenced patent or application.

The method steps recited in the instant claims are deemed essential subject matter to practice the claimed invention. Thus the attempt to incorporate subject matter into this application by reference to non-patent publications is improper. In order to provide the proper antecedent basis for these method steps, Applicant should amend the specification based upon the non-patent literature incorporated by reference. Applicant is reminded however that mere reference to another application, patent, or publication is not an incorporation of anything therein into the application containing such reference for the purpose of the disclosure required by 35 U.S.C. 112, first paragraph. In re de Seversky , 474 F.2d 671, 177 USPQ 144, (CCPA 1973). In addition to other requirements for an application, the referencing application should include an identification of the referenced patent, application, or publication. Particular attention should be directed to specific portions of the referenced document where the subject matter being incorporated may be found.

If the specification is amended to incorporate these method steps, Applicant is also reminded to provide a Hawkins-type declaration.

Thus for the reasons set forth supra, the specification stands objected to for failure to provide antecedent basis for the claimed subject matter.

6. Applicant's amendment, filed 11/7/01, has obviated the previous rejection of claims 1-2 and 9-11 under 35 U.S.C. 112, second paragraph.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Applicant's amendment, filed 11/7/01, has obviated the previous rejection of claims 2, 5 and 8 under 35 U.S.C. 112, first paragraph, enablement.

9. Claims 1 and 9-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody to the full length polypeptide of SEQ ID NO:3 or an immunogenic fragment thereof; does not reasonably provide enablement for an antibody to "a polypeptide having at least 90% sequence identity to the full length of the sequence of SEQ ID NO:3". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's amendment, filed 11/7/01, has obviated the rejection of record with respect to the issue of "a biologically active fragment".

Applicant's arguments, filed 11/7/01, with respect to the remainder of the rejection regarding an antibody to "a polypeptide having at least 90% sequence identity to the full length of the sequence of SEQ ID NO:3" have been fully considered but have not been found convincing, essentially for the reasons of record in Paper No. 6.

Applicant argues that because the polypeptide having at least 90% identity is naturally-occurring, it would not require undue experimentation to make such a polypeptide.

However, in the absence of some recitation of function possessed by a polypeptide having at least 90% sequence identity to the full length of the sequence of SEQ ID NO:3, the specification does not appear to provide sufficient guidance as to how one of skill in the art would use an antibody to such a polypeptide, even if the polypeptide were naturally-occurring. As previously noted Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000, of record) teach that even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. A person of skill in the art is not enabled to use an antibody to "a polypeptide having at least 90% sequence identity to the full length of the sequence of SEQ ID NO:3"; as encompassed by the full breadth of the claims as currently recited. Thus the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

The rejection is maintained.

10. The previous rejection of claims 1 and 9-11 under 35 U.S.C. 112, first paragraph, as lacking adequate written description is withdrawn.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Bentlage et al. (Biochimica Biophysica Acta 1995; 1234:63-73, of record, see entire document).

14. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walker et al. (J. Mol. Bio. 1992;226:1051-1072, IDS #2), in view of Bentlage et al. (Biochimica Biophysica Acta 1995; 1234:63-73, of record), and in further view of Ramakrishnan et al. (US Pat No. 5,817,310, or record).

15. Applicant's arguments, filed 11/7/01, consider the rejections under 35 USC 102(b) and 35 USC 103(a) together, so the response to those argument has been set forth together below. The full text of the rejections of record may be found in Paper No. 6.

Applicant's arguments, filed 11/7/01, have been fully considered but have not been found persuasive for the reasons of record in Paper No. 6.

With respect to the rejection under 35 USC 102(b):
Applicant first argues that Bentlage et al. does not teach an antibody that "specifically binds" to a polypeptide comprising SEQ ID NO:3 because in order to "specifically bind" an antibody must bind the recited polypeptide, but not other polypeptides.

Applicant also argues that Bentlage et al. describe in Section 2.4 on page 65 that the antibodies produced in rabbits "showed a reaction with approximately 10 subunits of Complex I preparation from bovine and human heart tissue" and Bentlage et al. therefore do not describe an antibody that specifically binds SEQ ID NO:3.

However, Applicant appears to be arguing a limitation not claimed and not supported by the specification as filed by asserting that "specifically binds" means that an antibody must bind only the recited polypeptide. In addition, Applicant's argument attempts to limit the term "specifically binds" in a manner inconsistent with the well-known and art-recognized specificity of antibody interaction with epitopes defined by particular amino acid sequences. That an antibody binds to more than one protein sequence does not mean that the antibody does not "specifically bind" both proteins.

Further, it appears that Applicant is disregarding that "a polyclonal antibody" was known in the art at the time the invention was made to be inherently a mixture of many different individual antibodies elicited by the immunizing antigen (in contrast to a monoclonal antibody). The term "polyclonal antibody" was recognized in the art at the time the invention was made to refer to a population of antibodies, each of which "specifically binds" various antigenic epitopes present on the immunizing antigen. Thus when the antigen has multiple immunogenic epitopes present on multiple polypeptides that make up the antigen, as is the case when the multi-polypeptide Complex I is used as the antigen; "a polyclonal antibody" produced by such a method would inherently include individual antibodies that specifically bind various antigenic components of Complex I, as shown by the several polypeptides recognized by the "polyclonal antibody" used in Figure 4a. That multiple polypeptides are recognized does not mean that the antibodies are not each specific for that particular polypeptide; instead it reflects inherent properties of "a polyclonal antibody".

Indeed, it is noted that even a monoclonal antibody may "specifically bind" to more than one polypeptide so long as both polypeptides share the antigenic epitope recognized by the monoclonal antibody: antibody specificity is inherently determined by the epitope, not by the polypeptide *per se*.

Thus the teaching of Bentlage et al. of a polyclonal antibody that binds a 15kD protein of human Complex I (see entire document, especially Section 2.4 and Figure 4a, arrowheads), anticipates instant claims 1 and 4.

Applicant's amendment does not alter the rejection of record.
The rejection of claims 1 and 4 under 35 USC 102(b) is therefore maintained.

With respect to the rejection under 35 USC 103(a):
In addition to the arguments addressed above, Applicant has further asserted that the teachings of Walker et al. do not make up for the deficiencies of Bentlage et al., presumably because Walker et al. do not teach a polypeptide comprising SEQ ID NO:3.

Applicant has argued that because the B15 polypeptide taught by Walker et al. is not 100% identical to the polypeptide of SEQ ID NO:3, there are many amino acid residues that would have to be identified before an antibody that "specifically binds" SEQ ID NO:3 could be produced.

As with the arguments discussed supra, this argument also relies on a limitation of the phrase "specifically binds" which does not appear to be supported in the specification as filed and is not consistent with the art-recognized usage of this phrase at the time the invention was made.

In addition, as previously noted based upon the alignment provided in Paper No. 6; besides having 75.8% identity, the B15 polypeptide of Walker et al. and SEQ ID NO:3 share several stretches of amino acid identity that are 5 amino acids in length or greater. Thus although Walker et al. do not teach SEQ ID NO:3, they do teach a polypeptide which comprises "antigenically-effective fragments thereof" of SEQ ID NO:3. In view of the numerous shared epitopes between the B15 polypeptide of Walker et al. and SEQ ID NO:3, an antibody that "specifically binds" one polypeptide would also "specifically bind" the other.

Combined with the teachings of Bentlage et al. and Ramakrishnan et al., it would therefore have been obvious to the ordinary artisan at the time the invention was made to utilize the instantly recited methods to produce antibodies of various forms that would specifically bind the polypeptide of SEQ ID NO:3 and formulate these antibodies in compositions comprising an acceptable pharmaceutical carrier, as discussed previously in Paper No. 6.

As also noted in Paper No. 6, the teachings of Bentlage et al. that antibodies against Complex I subunits were very useful for studying the molecular basis of mitochondrial encephalomyopathies (e.g., see Introduction and Discussion) would have provided the motivation for the ordinary artisan to apply the instant methods and produce such antibodies. In addition, given that Bentlage et al. also teach that antibodies produced using bovine Complex I as an immunogen react specifically with polypeptides from human Complex I (see especially Section 2.4 and Figure 4a, arrowheads); the ordinary artisan would have had a reasonable expectation that antibodies produced would have specifically bound the polypeptide of SEQ ID NO:3.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's amendment does not alter the rejection of record.
The rejection of claims 1-11 under 35 USC 103(a) is therefore maintained

16. No claim is allowed.

17. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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March 21, 2002

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